THE DIAGNOSTIC VALUE OF CALMETTE'S TUBERCULIN OPHTHALMO-REACTION

By J. Elliot Murray.

The oculo-reaction to tuberculin was as is now well known introduced last summer by Calmette, of the Pasteur Institute of Lille, as a diagnostic test for the presence of tuberculosis. That able worker in the field of tuberculosis claimed for it certain advantages over other tests hitherto in vogue. These may thus be summarized:

(1) It is absolutely safe; (2) it is so easy of application that any one can carry it out; (3) it produces no constitutional disturbance, an locally usually nothing more than a slight ocular discomfort and lacrymation; (4) it is as accurate and delicate as the hypodermic injection, if not more so.

Finding the presence of glycerine in the ordinary preparations of the tuberculin of Koch to have an irritating effect upon the human conjunctiva he precipitated the glycerinated product with alcohol and redissolved the deposit to form a 1 per cent. aqueous solution. He stated that one drop of this solution in the eye of a patient suffering from active tuberculous trouble was followed by a definite reaction which did not occur in the normal individual.

In from three to ten hours, sometimes rather sooner and not infrequently rather later, the positive reaction manifests itself. This consists at first of a slight injection of the conjunctiva near the caruncle, with a little lacrymation.

From first to last in the "slightest reactions" that is all that may be seen. In these light reactions the congestion is confined to the inner part of the conjunctiva, and unless it is looked for carefully it may be missed. It is, however, a quite characteristic redness, and can easily be recognized by comparing it with the normal untreated eye. The amount of reaction is most variable, and, so far as my experience goes, it does not bear a demonstrable relation to the severity of the lesion from a clinical point of view. Some of the most pronounced reactions I have seen were in cases in which there were no physical signs or clinical evidence of the presence of tubercle. We may get all degrees of inflammation, from the smallest amount of local conjunctival injection to redness extending over the entire eye, and having all the appearance of acute conjunctivitis. There is occasionally some purulent discharge, and much photophobia and swelling of the caruncle. None of these reactions, even the most severe, have given rise to any trouble, and almost all have, in a period of from two to ten days, completely cleared up. This occasional over-violent reaction is the only drawback to the test that I have observed. Perhaps it may be eliminated by giving always in the first instance a weaker solution, say a 1 in 200, as a preliminary test..

The applicability and the delicacy of this test depends on the integrity of the eyes. Any ocular lesion, whether it be acute or chronic, contraindicates its employment. In my own cases only eyes that were perfectly healthy were subjected to the test. Brunetière thinks the test may be applied if one eye be intact by dropping the solution into the sound eye. But as the reaction, especially when slight, is only appreciated by comparision with the sound eye, this does not give satisfactory results. The majority of the patients did not complain of any pain, but noticed some slight discomfort in the inoculated eye, best described in their own words as "it feels as if there was a little grit in my eye;" there was also a general complaint of watering of the eye, accompanied by epiphora, which lasts for a varying period and is of varying severity, corresponding usually with the severity of the reaction. In only the most severe reactions was there any purulent discharge; but nearly all the patients giving the reaction complained either of a slight amount of discharge or else that their eyelids on the inoculated side were glued together when they awoke on the morning following the day when their eyes were inoculated. It was probably due to the fibrinous exudation which occurs normally during this reaction and not to any purulent discharge.

Five patients complained of a little intolerance of light; they were those who gave the most severe reactions. I have noticed that in many cases the first indication of any reaction was afforded by the plica semilunaris, which is situated just to the outer side of

the caruncle, and the swelling and slight reddening which this undergoes occupies a fairly prominent place throughout the whole of the reaction; In one case this fold was the only part of the conjunctiva to show any signs of reaction, and in this particular individual it was evidenced not so much by reddening (present only in a slight degree) as by swelling, especially obvious when the two eyes were compared.

Dr Leon Petit of Lille says that this test enables us to certify a cure when accomplished. It puts into our hands an easy, harmless and efficacious means of detecting infected amongst a number of non-tubercular persons. It will, therefore, be of obviously great utility both in public and private work.

The comparative delicacy of the test may be gauged from the results published by Letulle, who, in 75 tuberculous cases tested, got a positive ophthalmo-reaction in all except 3; 2 of these 3 were moribund, while the third recovered. These results are interesting. If, during a chronic tuberculosis, any antitoxin is, as one would expect it to be, devoloped, then the failure of the reaction in the 2 of Letulle's cases may have been due to an immunity imparted to the tissues, or else to the fact that vitality was too low to give any inflammatory reaction.

It is clear that if this test proves, on further experience, to be reliable, it will be a valuable aid to the early diagnosis of tuberculosis in obscure cases, and more especially in dealing with children. The success of modern methods of treatment depends on the early diagnosis of phthisis and other tuberculous affections. When a lesion is presenting clinically well-marked physical signs and symptoms, and its tuberculous nature has frankly declared itself, it is often too late to intervene

with any prospect of success.

Undoubtedly a far larger proportion of the apparently healthy than we imagine are the victims of latent tuberculous affections. The observations made in the postmortem room, or when the abdomen is opened for surgical purposes, amply bear this out, and the frequent evidence we have of bygone and completely-healed tuberculous lesions demonstrates that tuberculosis is an eminently curable disease. Any test that can help us to make our diagnosis earlier, and so to institute treatment at a stage when it would be effective, would be of the greatest importance to the physician and the public. Probably if this disease is to be stamped out, our best chance of exterminating it is to recognize it in the young and in its preclinical stage. If segregation of the tuberculous ever becomes a practical question, might not school children who exhibited suspicious symptoms and who gave a positive ophthalmo-reaction be segregated and kept under observation?

Some rather interesting points suggest themselves from a study of my results. In a few cases not suspected to be tuberculous, but whose family history was bad, I have obtained pronounced reactions. Is it possible that this reaction not only reveals the presence of an actual lesion, but also a condition of tissue which is susceptible to the devolopment of tuberculosis? What is the meaning of this reaction? Clearly to the conjunctiva of the tuberculous it is an irritant. To the eye of the healthy it is bland. Is the tuberculin elaborated in the living tissue the same as that manufactured in vitro? One would expect that tuberculin instilled into the eye would "react" only in the healthy, for is not the reaction a sign of tissue resistance that

we would expect to find better developed in the healthy than in the unhealthy? It seems apparent that tuberculin, or some other toxin developed in the tuberculous, imparts to the tissues a resistance to tuberculin, as expressed by the inflammation in the eye or skin, that is absent in the healthy. Von Pirquet holds that the reaction is due to the presence of an antibody.

Chantemesse in a paper read at the Académie de Médecine (July 1907) described an analogous reaction in Enteric Fever to a strong solution of Typhoid Toxin. The toxin was precipitated by absolute alcohol and the powder obtained dissolved in distilled water. In enteric cases the reaction was very pronounced, maximum intensity being from 6 to 12 hours. There was hyperaemia, lacrymation, and a sero-fibrinous exudation - in all respects very like the ophthalmo-reaction of Calmette. No constitutional disturbance was observed. Chantemesse could not affirm whether this reaction is, or is not an early sign of enteric, but the reaction has been got in the eye of rabbits injected 48 hours previously with enteric bacilli.

There seems ample evidence that the reaction in cases of tuberculosis is nearly constant. There can be little doubt that before long, after the present wave of enthusiasm has died down, the inevitable swing back of the pendulum of medical opinion will take place, and that a period of almost two years must elapse before we will be able to put a fair and just estimate on the value of this method. Meanwhile this much seems to be demonstrated -

1. That except in very grave or moribund cases of tuberculosis the reaction can be obtained.

2. That although it is usually confined to one eye it is not always so, for the characteristic conjunctivitis sometimes appears in the non-inoculated organ.

3. That no relationship exists between the severity of the local reaction obtained and the acuteness or chronicity or type of the disease.

4. That the reaction is very rarely found in persons who are not the subjects of tubercular disease; and that,

5. Consequently the test, although absolutely reliable, is of considerable value.

"La Presse Medical" 13th July 1907.

An article by Calmette, Breton, Painblau and G. Petit who give their results in different hospitals.

In children out of 18 cases 9 were positive, they included Phthisis Pleurisy, Tubercular Meningitis.

It is interesting to note that these observers got a positive reaction in tubercular meningitis as many have got a negative result in that condition.. 9 negative cases included typhoid, rickets and hereditary syphilis.

In a "Diseases of the skin" ward a positive reaction was got in a case of lupus of the nasal mucosa.

In adults out of 33 cases, 17 were positive. All were cases of Phthisis in different stages. 16 were negative. They included Tabes, Sciatica, Bright's Disease, Erysipelas, Mitral disease, Hysteria, Rheumatism, Cancer of Oesophagus.

In another hospital out of 10 cases, 4 were positive. There were tubercular glands in groin, and suppurating glands in the neck. 6 were

negative including arthritis of the knee, eczema and syphilis.

In a consumptive hospital out of 9 patients 7 were positive, all in the first stage of Phthisis. 2 were negative. These had slight consolidation at one apex and were thought to be cases of healed tubercle.

Out of a series of 21 cases, 8 were positive, all with marked signs of tubercle. 13 were negative, including Emphysema, Bronchitis and neuralgia.

A further series of 18 cases, 12 were positive, 8 showed marked signs of Tubercle, 3 showed no clinical signs of Tubercle and one was an emaciated alcoholic. 6 were negative - none showed any sign of tubercle.

Out of 10 cases 5 were positive, one of which was very slight - a case of aneurysm which was being treated with Iodide of Potassium. 5 were negative and had no clinical evidence of tubercle.

Out of 22 cases, 14 were positive including Phthisis, Hip joint disease and Tubercular Peritonitis. 8 were negative including appendicitis, pneumonia, and myocarditis.

In all 321 observations were made and not a single bad result is recorded.

"La Presse Medical" 18th September, 1907.

An article by Olmer and Marcel Tessas who found the Calmette ophthalmo-reaction much more reliable than the cutaneous reaction. They got more positive results with the former than with the latter.

In the same Journal, 19th October, 1907 M. Mentoux says he tried the reaction in 200 apparently healthy children and got a positive reaction in 8% of cases.

In the same Journal, 26th October, 1907, Monsieur Jean Lépine tried the reaction on lunatics and discovered the great diagnostic value

of the ophthalmo-reaction in Psychiatry especially when there is a doubtful etiology of the mental condition.

Another article in the 2nd November number of the same journal by M. Kalt, who reports two cases of evil effects after using ophthalmo-reaction in eye conditions.

The first was a man of 64 who had an Iritis-Choroiditis of the right eye and a Sclero-Keratitis of the left eye. The ophthalmo-reaction was followed by a very severe conjunctivitis and his other eye conditions were so aggravated that he became blind, only being able to distinguish light from darkness. This case should be a warning not to try the ophthalmo-reaction unless the eye is absolutely healthy.

The second case was that of a child with Tubercular Iritis. The condition was much aggravated after the ophthalmo-reaction had been done.

"New York Medical Journal"- De Lapersonne concludes that the ophthalmo-reaction is not by itself a source of danger to the eye and that the rare cases in which accidents have occurred simply call for some counsels of prudence. He says that the test should never be made until after a thorough examination has been made of the eye of the patient. In Ophthmology he thinks its use will be very limited. It will not serve for the diagnosis of superficial or deep lesions of the eyeball, but it may for the diagnosis of diseases of the lids, lachrymal passages and orbits. He does not think it should be used in old patients.

The following extract is from "Le Bulletin Medical." The article is written by M. le Dr J. Comby, Physician to the Sick Children's Hospital, who says-

"I have only twice seen among the young patients in my Hospital"

"any serious result from the ophthalmo-reaction, not only was the reaction very violent and marked by considerable swelling of the eyelids but it was of long standing."

This was when Comby used 1 in 100 solution of Tuberculin. After this he always used 1 in 200 solution first of all, and if he got no reaction, then used 1 in 100 solution, but he says he has never got a positive result with 1 in 100 solution in any case which was negative with a 1 in 200 solution.

Comby describes 3 degrees which he got by using Calmette's Tuberculin test.

1. Réaction Légère, which is so slight that it requires some care in observation to see that it is positive. It is essential to compare the inoculated eye with the sound one. It sometimes is visible only when the inoculated eye is rotated outwards. Generally passes off in 2 days.

2. Réaction Modéré which is seen without difficulty. The internal half of the conjunctiva is injected. This passes off in from 5 to 7 days.

Réaction intense where the whole conjunctiva is involved and there is a good deal of oedematous swelling. There is sometimes a purulent secretion, Epiphora and a good deal of pain, sometimes conjunctival haemorrhages. It is rare to get this with a 1 in 200 solution.

Comby found that a great advantage of the ophthalmo-reaction is that it is purely local. He found there was no general reaction as that which follows subcutaneous injection of tuberculin.

Other observers say there is a slight temporary general reaction shown by a rise in temperature, but that the temperature soon comes down again.

Comby observed that if those cases which gave a positive reaction

were inoculated a second time, the reaction was always positive and of the same intensity. He also observed that if the reaction was negative, however often the person was inoculated again, the reaction was always negative.

He describes the value of the Ophthalmo-Reaction in Surgery and gives an interesting case as an example. A boy with hip joint disease which terminated in Ankylosis. The Calmette reaction was not known in the early stage, but was negative after ankylosis took place. Comby gathers from the negative result that the case was cured.

Comby performed 18 post mortem examinations on children whose ophthalmo-reaction he had done. In 8 cases which gave negative result there was no sign of Tubercle. In 10 cases which gave positive result, there were signs of Tubercle in all.

He explains how negative results may be produced when positive ones are expected. Firstly the observer may not take sufficient care to see that the drop goes into the eye of the patient. Especially is this liable to occur in the case of children who are constantly moving and will not open their eyes. Secondly the child may cry and the tears may wash out all the solution.

So in children it is advisable to do the test a second time, if it is negative the first time, and to be very careful that the drop goes into the eye.

In summing up Comby says that in 24 cases in which he used a 1 in 100 solution he had 2 what he terms "bad results" but with a 1 in 200 solution he inoculated 276 children and got a positive reaction in 99 and a negative in 177, and had not a single accident.

There are certain advantages to be got in testing all children for the ophthalmo-reaction, namely that you can find out tubercle where there is no suspicion of it clinically, and secondly you can satisfy yourself that a suspicious case with a bad family history is free from tubercle if the reaction is negative. In this way a great deal can be done to prevent the spread of Tuberculosis. Children giving a positive reaction can be sent to the country and kept in the open air.

In Tubercular families and in hospitals children giving a positive reaction should be kept apart from children who give a negative reaction.

Extract from an article in the "Lancet" February 8th, 1908.

M. Calmette said that in the short time which has elapsed since he communicated his discovery to the Academie des Sciences (June 17th 1907,) the almost absolute accuracy with which the reaction reveals the existence of tuberculous lesions in evolution, although manifested by no clinical signs, has been confirmed by numerous observers. Many observations have shown that the newly born children of tuberculous mothers do not give the reaction. On the other hand, infants at the age of from 1 to 2 years react in the proportion of 3·42 per cent. and the percentage increases rapidly with age. It is 5·26 at the ages of from 2 to 5 years, 13·5 at the ages of from 6 to 10, and 14·9 at the ages of from 11 to 15 years. These results are in accordance with the observations of Bang and Nocard that in cattle tuberculosis is scarcely ever congenital. By repeating the test sufficiently often M. Calmette suggests that the exact time at which tuberculosis attacks a child may be ascertained. By studying at the same time the conditions of the family and the food supply he thinks that the part played by family contagion (contagion familiale) and by

the milk of tuberculous cows may be ascertained. By applying the test periodically to a family, or at least to those members in whom tuberculosis is feared, the infection may be detected at an early period, before even any clinical sign is perceptible. The patient may thus be isolated from his family and sent to a sanatorium and treated at the most favourable time. At the anti-tuberculosis dispensary of Emile Roux at Lille the test was applied to the children of families the members of which were under treatment. Thus children apparently healthy were ascertained to be tuberculous and were sent to the country and placed in the best hygienic conditions. At the same time they continued their school studies until the instillation of tuberculin into the eye, repeated every two or three months, no longer gave a reaction. They were then sent back to their families. M. Calmette thinks, with Marfan, that experiments on animals and the observations on patients discharged several years from sanatoriums show that the complete cure of chronic tuberculous glands confers immunity against tuberculosis. He therefore hopes that a great number of these children will remain immune. The reaction would be equally useful in the examination of pupils who seek admission to schools and are suspected to be tuberculous. Tuberculous pupils could thus be arrested "on the threshold"; in the army and navy the test could be put to a similar use. Professor Simonin of the military hospital of Val-de-Grâce has recently stated that the reaction reveals latent or insidious tuberculosis not evident clinically which provokes distant functional troubles of unknown causation. It thus enables patients suffering from dyspepsia, palpitation, neurasthenia, "atonic rheumatism," and so on,

to be discharged from the military hospitals which they encumber. M. Calmette finally claimed that thanks to its fidelity and harmlessness, attested by more than 10,000 observations published in all countries, his reaction merited the confidence of clinicians and could play a great part in the social struggle against tuberculosis. By its use in families, in schools, in the army, in hospitals, and in all collections of persons those who were bearers of active tuberculous lesions could be detected.

Extract from the New York Medical Journal, February 1st, 1908.

Mainini asserts that 1. the cutaneous as well as the ophthalmo-reaction is positive in persons with positive tuberculosis with great constancy, with the exception of very advanced cases; (2) the specifity of this reaction is probable for many reasons though not yet proved. (3) In individuals not suspected of tuberculosis the cutaneous reaction has perhaps a higher value than the ophthalmo-reaction. (4) Under the assumption that the reaction is specific this contradiction appears that the ophthalmo-reaction points to an active tuberculosis chiefly while Von Pirquet's reaction indicates rather a latent focus. Wiens and Gunther state that they obtained in a number of cases very serious changes in the eye from the instillation of a 1% solution of tuberculin as recommended by Calmette and allege that this procedure is not so harmless and unimportant as has been supposed.

Klieneberger investigated the ophthalmo-reaction in 61 cases, 9 tuberculosis, 6 suspicious and 46 presenting no clinical signs of tuberculosis. All 9 tuberculous patients reacted positively. Very severe inflammatory symptoms appeared in one case of pulmonary tuberculosis.

Of the 6 suspicious cases 2 reacted positively. Of the 46 cases presenting no clinical evidence of tubercle 36 reacted positively. A severe conjunctivitis was induced in 16. In 5 there was considerable swelling of the lid, Diffuse haematoma , and chemosis of the conjunctiva, conditions which rendered necessary a long course of treatment.

Smithies and Walker describe their experience with the Calmette Ophthalmo-reaction to tuberculin. They had 185 cases,clinically diagnosticated as tuberculous cases, 176 of these gave a positive reaction. 9 negative. Of 28 doubtfully tuberculous cases 21 gave positive reactions, 7 negative. Of 188 persons suffering from disease not tuberculous, and including a fair proportion of apparently normal individuals, 186 gave a negative reaction and only 2 positive.

The authors are convinced that the ophthalmic reaction as directed to be practised by Calmette and others is of undoubted service in the diagnosis of Tuberculosis. In no case where its work could be tested clinically by the finding of tubercle bacilli, did they fail to obtain decided ocular manifestations following the instillation of the tuberculin. This reaction did not follow when instillations were made in the case of 126 individuals affected with disease other than tuberculosis. It was not obtained in 74 apparently normal adults.

The fact that a reaction thus appears does not mean that the subject is affected with an active tuberculous process, although the evidence is strongly in favour of such.

The hypothesis advanced by the authors is as follows:- The inflammatory changes in the eyes of tuberculous individuals following the instillation of tuberculin suspensions, is due to the slight

stimulation of the hypersensitive cells forming protective substances, with the production of an excess of antibodies. These antibodies so produced by acting on the tubercle bacilli or fragments of such enmeshed in the conjunctiva, liberate sudo-toxines which are capable of producing the inflammatory changes commonly observed.

Professor F. de Lapersonne in La Press Medicale, 7th December, 1907 quotes the following:

A man 37 years of age with Tubercular disease of the knee had ophthalmo-reaction done and did not react for 3 weeks. He had an intense circum corneal injection especially in the lower part. Felt his eye gritty, had photo-phobia and trouble with his sight. Treated with Argyrol cocaine and atropine, hot compresses. It took a long time to disappear but his sight was not interfered with.

Professor Lapersonne found that in cases where there was a marked conjunctivitis the best cure was Argyrol 20% dropped into the eye 4 times a day.

The following statistics are in cases which are known to be tubercular:-

Letulle out of 75 cases got a positive reaction in 72. 2 of the remaining ^were moribund and the other did not show T. B. post mortem (Lancet)

M'Lellan out of 25 cases got a positive reaction in 23. In one of the others, the child cried a good deal, so the tuberculin may possibly have been washed out of the eye. (British Medical Journal)

Webster and Kilpatrick out of 43 cases got a positive result in all of their cases. (British Medical Journal)

Austin and Grunbaum got 18 positive results out of 20 cases tested.

Prouff got 69 positive reactions out of 70 cases. the one negative

case was moribund.

Eyre got 13 positive results out of 13 cases tested.

From these statistics it is seen that in 246 cases known to be tubercular, 238 gave a positive reaction, the majority of the remainder being moribund.. This speaks for itself, if one gets a positive reaction in over 96% of the cases which are known to be tubercular, it stands to reason that this is a most valuable test for tuberculosis in Man.

Use of Calmette's Tuberculin Test in Eyework.

To show the value of Calmette's Tuberculin Test in connection with Diseases of the Eye , I quote from an article by Sydney Stephenson:

Apart from lesions of the eye recognized by all competent observers as tuberculous, there are several others - especially chronic irido cyclitis, scleritis, and some forms of choroiditis - of which the tuberculou origin is as loudly proclaimed by one school as it is decried by another. The preponderating part unquestionably played by syphilis in the production of many of these affections has, perhaps, tended to render some of us a little blind to the influence of other causes, prominent among which, as I believe, stands tuberculosis. How often do we meet with disseminated chorciditis, indistinguishable by the ophthalmoscope from the form due to syphilis, in patients in whom there is no evidence whatever of a specific taint, acquired or inherited. I feel tolerably confident that the systematic employment of the ophthalmo-reaction will show that no small number of such non-syphilitic cases are in reality due to tuberculosis.

My personal experiences with the Calmette serum are far from

complete, but up to the present time I have applied it to the eyes of upwards of thirty patients, all of whom were suffering from some disease or affection of the eye. The more important cases may be briefly described as follows:

1. Phlyctenular (Eczematous) Conjunctivitis and Keratitis.- The tuberculous origin of these common affections of the eye has been suspected for years, and the view is widely held at the present day that they are caused by a tuberculous toxin circulating in the blood stream. The Calmette serum was applied to the eyes of six children, all of whom had been affected with long-standing and relapsing ulceration of the cornea. Only two of the patients manifested tuberculous lesions elsewhere. The ophthalmo-reaction however, was obtained in every instance.

2. Choroiditis.- The serum has been applied in 3 cases of choroiditis in young women, free, as far as could be ascertained, from evidences of syphilis, acquired or inherited. Two of the patients were single and the third married. The choroiditis was bilateral in 2 and unilateral in 1 case. The choroidal lesions were of long-standing. In Case No. 1 the gross disseminated choroiditis presented no ophthalmoscopic features whereby it could be differentiated from a syphilitic process. In Case No. 2 the changes effected almost exclusively the central region of the fundus. Case No. 3 showed in the central region of one fundus a map-lika area of choroiditis, and while under observation a second area of disease made its appearance below the optic disc. Each eye was myopic to the extent of 3·5 D. In each of these three patients the ophthalmo-reaction was obtained, although in none had a tuberculous focus been found by clinical examination.

3. Tubercle of Iris,- A female, aged 12 years suffering from a disabling affection of the left eye of nearly six months' duration. The anterior chamber of the left eye was almost filled with solid-looking, yellowish-gray exudation, so that the pupil could be recognized with difficulty. The eye was somewhat reddened, tension was slightly minus, and sight was equal only to counting the outspread fingers when held close to the child's face. No clinical signs either of tubercle or of syphilis. A well-marked reaction came on in nine hours, and persisted for twenty hours.

4. Tubercle of Cornea.- A girl, aged 12 years, with the history that her right eye had been more or less inflamed for about two months. The child's mother suffered from phthisis pulmonalis, and one of her brothers had died at 9 months "with lungs badly affected". The patient herself "had brought up blood" on one occasion. Slight photophobia and patchy ciliary redness. Several curious looking deposits lay at different levels in the substance of the cornea, where they formed a kind of mosaic. Their colour was greyish-white, and they might be compared with drops of cold mutton fat. In addition, the rest of the cornea was more or less hazy. No deposit, such as those on which great stress has recently been laid by Dr Stock could be recognized on the anterior surface of the iris. The pupil responded imperfectly to atropine, which disclosed the existence of posterior synechiae. Although a reflex could be obtained through the upper part of the pupil, yet no details of the fundus could be made out. Provisional Diagnosis: Tubercle of cornea, probably secondary to a similar condition of the iris and ciliary body. A reaction was noted in five hours, and this had disappeared completely

thirty-one hours after the serum had been used to the eye. Dr Stephenson mentions several other cases in which the Calmette reaction was of diagnostic value, but these are sufficient to confirm this statement.

The following observations were made at the Crossley Sanatorium for Consumption during the four months, November, 1907, to February, 1908.-

The tuberculin employed was obtained from the Pasteur Institute, Lille. The same pipette was employed for each instillation thus ensuring accurate and identical dosage. All the patients were under precisely similar conditions. All were under observation from hour to hour from the time of instillation. When no reaction was obtained in the first instance, a second instillation was administered after a fortnight's interval. When this also proved negative, a third instillation was given after a similar interval.

Of 106 cases examined, 2 only failed to give a reaction even after three such instillations.

Of the 104 cases in which a reaction was obtained tubercle bacilli were found in the sputum in 83; of these 78 reacted to the first application, 5 only reacted to the second. These 5 cases were all of an advanced type. In 2 the larynx was secondarily involved, and in 2 others there was morbus coxae in addition to extensive pulmonary lesions.

In 26 cases no tubercle bacilli could be found in the sputum even after repeated examinations; of these, 10 reacted to the first application, 6 to the second, and 5 to the third. Of the 6 cases which only gave a reaction to the second application, 3 were of a very early type and could be considered as being apparently cured, the physical signs

being consistent with the existence of healed foci of tuberculosis. One had tuberculosis of the os calcis with slight involvement of the right apex; one had marked lesions in both lungs, and the last of this series was an old case which had been under observation during the past five years. Of the 5 cases which only gave a reaction to the third application all exhibited definite physical signs with lesions of limited extent in one or other apex. The 2 cases which gave no reaction to the tuberculin and in whose sputum no tubercle bacilli could be demonstrated are added.

H. M., aged 18, had all the physical signs and symptoms of bronchiectasis, probably of pneumonic origin.

S. F., aged 13, had previously had a pneumococcal empyema, and was affected with marked scoliosis.

It is doubtful whether any relation exists between the intensity of the reaction on the one hand, and the activity of the disease or the extent of the lesion on the other. We noted, however, that in some cases with physical signs of early or healed lesions the reaction was sluggish, sometimes delayed, and perhaps only positive on the second or third application. In several advanced cases with evidence of marked pleural thickening, and in some cases fluid, the reaction was also delayed until the second or third application, when it developed a severe type.

This is what one would expect, as in these early cases in which the reaction was delayed the disease must have been latent; in the advanced cases such a minute dose of tuberculin was not likely to elicit a response at the first application. It has been universally recognized that in very advanced or moribund cases no reaction is obtainable.

The following is from an article in "British Medical Journal", March 28th, 1908, by Dr H. de Carle Woodcock of the Leeds Hospital for consumptives:-

I have most carefully read Professor Calmette's article in International Clinics, and I have tried the ophthalmic reaction in 200 cases, including both hospital and private patients.

The reaction shows best in twenty-four hours, in some few exceptional cases it appears even after a longer interval than twenty-four hours. Among my cases were many of surgical tuberculous disease (joints or glands). These cases gave a reaction quickly, and the effects were slow in passing away. Patients with coincident disease of the eye or lids reacted violently, and it is interesting to note that in one case of choroiditis said to be syphilitic, one of iritis said to be rheumatic, one of slight conjunctivitis, two of severe corneal ulcer, and one case where the patient was constantly using his eyes all day, the reaction was not only violent, but continued for a period of ten days. These patients complained, in one case bitterly, of the pain and inability to use the eye. Of these patients with eye defects or lesions, two gave no other indication of tuberculosis apart from this ophthalmic reaction.

Two of my patients with T. B. and with physical signs of pulmonary disease gave no reaction with one application of Calmette's fluid; in one of these cases a repetition of the test caused the reaction to appear. I was able to test 5 children in the workhouse through the courtesy of Dr Isaac Taylor of Leeds, and in these the reaction was slight, with one exception. Each case was undoubtedly tuberculous, but each was so tearful whilst the tuberculin was being applied that

possibly the tears washed out the testing fluid.

Many people react who are not tuberculous according to the ordinary acceptation of the term. Three people in the family of a friend reacted although in good health. Two of my patients showed an increase of temperature (from normal to 102°F. in one case,) many suffered from headache without temperature. Of course, the reaction does not give any help in locating the disease, and the mistake might easily be made and a wrong conclusion drawn if the patient were suffering, say, from bronchitis and a hidden tuberculous focus in addition.

I have only tried the test once in the case of the dying, and in this case there was no reaction.

For some time I have been using another form of test. I put two small blisters on to the back of the chest; after the blisters have risen I give two days of water dressing to lessen the hyperaemia, and then to one of the blistered surfaces I apply Koch's T. R. new tuberculin in its concentrated form, the patient lying exposed until the surface has dried. This takes about half an hour. I then put a dressing of sterilized lint on to the two surfaces, and in twenty-four hours I compare them. The surface which has been treated with tuberculin is then rosy and red with a blush on its circumference, and the untreated surface is comparatively pale. This method has proved satisfactory, and it has not caused the annoyance to the patients which has so often followed the application to the eye. Its disadvantage is the time required, consequently in hospital patients I am more inclined to use the blister test, in out-patients the Calmette.

The great question is, Do these reactions occur ever in non-tuberculous patients?

Dr Lecky of Brighton contributes the following:-

In view of the memoranda and correspondence on Calmette's reaction published recently in the British Medical Journal, the following figures are of interest. They are taken from a short note on Calmette's reaction which I have contributed to a forthcoming issue of Public Health. Up to the middle of January I collected all the published statistics of this reaction. Of 491 cases of definite tuberculosis, 463 (94·3 per cent) gave a positive reaction. Of 610 cases of people not giving any evidence at all of tuberculosis, 563 (92·3 per cent) showed a negative result. There are two other classes where the reaction is being tried - namely, those possibly tuberculous and those probably tuberculous; but the figures under these headings are necessarily of little use at present in estimating the value of the test.

Use of Calmette's Tuberculin Test in Surgery.

1. Boy T.A. aged 7 suffering from frequency of micturition and pain. Albumin, blood and pus in urine.

Differential Diagnosis lay between tubercule of bladder and chronic cystitis. Calmette's reaction was negative. Bacteriological examination showed B. coli communi.

2. Girl D. L. aged 3 After measles suffering from pain and abscess over scapula. She had two chronic ulcers which had sinuces reaching to scapula.

Diagnosis was chronic Ostromyelitis of scapula possibly tubercular in origin. Calmette was negative. Bacteriological examination showed the condition to be staphylo coccal in origin.

3. Woman, Mrs T. aged 57.

Very marked Tubercular history. Cervical and inguinal glands much enlarged. Disease of bone and joints very extensive necessitating amputation of both legs above the knee. Calmette's reaction was very marked. Came on in 12 hours and lasted for a month.

4. Girl, E. M. 32 Complained of enlarged glands in neck. These were removed and found to be tubercular on microscopical examination. Calmette's reaction was very slight and passed off in 48 hours.

5. Man, H. G. Able-bodied seaman and healthy; good history. complained of stricture. Calmette's reaction was positive - very marked conjunctivitis after 36 hours which lasted for 14 days. There was no evidence of T. B. anywhere in his body.

6. Mrs N. 58 operated on for umbilical Hernia. Healthy woman, good family history. Gave marked Calmette reaction in 36 hours. On examining her lungs, slight dulness at left apex, high pitched bronchial breathing and a few crepitations on deep inspiration.

7. Boy, G. S. aged 13 with frequency of micturition whose bladder capacity was 3 1½. Pus in urine, no blood. Right kidney enlarged. Calmette's reaction was positive in 12 hours. Improved with iodoform injections into the bladder.

Medical Cases:

Spastic Paraplegia due to Pott's Disease.

Boy, aged 14. Complaint Inability to walk, pain in the back. Duration 7 months. History - Gradually lost power in limbs, unable to flex the thighs; ocasionally severe pain in the back. On admission was unable to walk owing to spasticity. Previous health. Always delicate child. Had been in hospital two years before for a lump in

his chest which he says was opened under chloroform. Family history, no tuberculosis in family history except that a sister of patient's died from multiple abscesses which may have been tubercular. On admission, delicate looking. Unable to walk. Discharging sinus on left side of chest. Prominence of 3rd D. V. but no pain on pressure. Nervous System.- Knee jerkes, achilles jerks exaggerated greatly. Patellar and ankle clonus. Double Babinski, very well marked. Spasticity of muscles of lower extremity. Lungs.- No sign of Tubercle. Calmette + in 5 hours, well marked conjunctivitis. Lasted 3 or 4 days. 2nd day lids glued together with discharge from eye.

Asthma and chronic Bronchitis.

Man, 68. admitted complaining of severe cough and dyspnoea. A typical case of chronic Bronchitis and asthma. No evidence of Tubercle in his lungs. Sputum examined several times and no T.B. found. Calmette's reaction was positive in 24 hours and gave a very marked conjunctivitis. Three days afterwards a conjunctivitis of equal severity started in the other eye and it was a fortnight before the conjunctivitis cleared up. This secondary conjunctivitis was probably due to his inoculated eye being rubbed with his hand or handkerchief and accidentally rubbing the other eye and thus inoculating it.

Phthisis and Tubercular Peritonitis.

Man 47, admitted complaining of swelling of abdomen and general weakness. Cough and spit. On examination his abdomen was prominent and tense. There was a distinct thrill on testing for free fluid. He was tapped and 3 70 fluid removed from his abdomen. Fluid contained lymphocytes in excess. No T.B. found. He had a very bad alcoholic

history and the difficulty was to determine whether this fluid was due to tubercular peritonitis or due to cirrhosis (alcoholic) of liver. The liver was enlarged. He had marked dulness at both apices, crepitations, high pitched bronchial breathing. T.B. in his sputum. Calmette was positive in 8 hours and gave a well marked reaction. The fact that he had tubercle in his lungs accounted for the C. R. being + so this reaction did not help in the diagnosis of his abdominal condition. The fact that the fluid had specific gravity of 1014 and contained excess of lymphocytes pointed to chronic Tubercular Peritonitis in spite of the fact that no T.B. were found, that the liver was enlarged and that he had an alcoholic history. Had he not had tubercle elsewhere, the Calmette reaction would have aided in diagnosis.

Phthisis.

Boy 19, complaining of cough, copious thick sputum sometimes tinged with blood. On examining him there was evidence of Tubercle in both lungs, more especially the right and a large cavity near apex of that lung. Heart much displaced to the right side. Calmette was positive in 12 hours, very mild reaction. T.B. found in sputum.

The interest of this case is the fact that the reaction was so mild notwithstanding the advanced tubercle. Possibly later on there will be no reaction, as the case will be too far advanced to react.

Phthisis: Man, 32, complaining of cough and sweating at night. Pain in chest. Evidence of extensive tubercle of left lung, a good deal of dry pleurisy on left side. T.B. found in sputum. Calmette positive in 8 hours.

Pleurisy with Effusion. Phthisis:

Boy, 11, complaining of pain in his chest and cough. On examination was found to have pleurisy & Effusion and extensive tubercle of both lungs. Calmette was positive in 6 hours; reaction not well marked but next morning a muco-purulent exudate glued the eyelids together. this disappeared in the course of a few days.

Phthisis.

Girl 22, complaining of shortness of breath, cough, pain in back. Had a cavity at left apex, evidence of tubercle at right apex. T.B. found in sputum. She also had a good deal of albuminuria.

Calmette positive in 12 hours and remained for 10 days.

Pleurisy with Effusion.

Girl 12, complaining of pain in the chest and cough. On examination she was found to have extensive pleural effusion, causing displacement of the heart and collapse of the lung. Reaction was positive in 8 hours and was very slight, confined only to the inner canthus.

Man, aged 34. A case of peroneal type of progressive muscular Atrophy who had had early phthisis at right apex some years ago. Had led an open air life since. His cough had disappeared and there was no evidence of active tubercle in his lungs.

Calmette was negative.

Spastic Paraplegia.

Boy, 19, admitted complaining of stiffness of the legs and difficulty in walking. On examination he was found to be suffering from Spastic Paraplegia. The cause could not be found. He gave a positive ophthalmo-reaction although there was no sign of tubercle to be made out. On tapping and pressing over his vertebral

column no pain was felt by him, but he stated that when working, if he stooped for a long time he felt a severe pain at the lower part of his vertebral column on straightening himself again. Whether this pain was muscular or due to disease of bone is not certain but the positive reaction is interesting.

Diabetes Mellitus.

Man, 38, suffering from great hunger and thirst and passing excessive quantity of urine. Urine contained 38 grains per ounce of sugar. There were physical signs of phthisis at both apices and T.B. were found in the sputum. Gave a very slight positive reaction.

Spastic Paraplegia.

Man, 24, suffering from well marked spastic paraplegia, duration 18 months. No sign of disease of bone. Syphilis 4 years before. Diagnosed as a gumma pressing on the cord. Calmette's reaction was positive. Well marked conjunctivitis. No signs of tubercle anywhere.

Lymphadenoma.

Man 36, Had enlarged glands removed from his neck 3 years ago. These were said to be tubercular by the surgeon who removed them, although as far as can be learnt there was no microscopical examination done at the time. Has now enlarged glands on both sides of his neck, in axillae and a few in the right groin. His temperature swings considerably. Calmette's reaction was done 4 times and was always negative. Blood showed 7,300 white cells per cubic mm.. Differential count showed 57% large lymphocytes. By excluding tubercle, the diagnosis lay between an early case of lymphatic leukaemia or lymphadenoma. Had a gland removed from the neck and it was found to have early

lymphadenomatous change.

The interest in this case is whether the glands removed 3 years ago were really tuberculous.

Pneumonia.

Boy, 21, a case of double pneumonia, who was at death's door for 4 days. His lung condition did not clear up and he was spitting up some thick pus. This was examined and contained pneumo-cocci, staphylo-coccus albus and Staphylo-coccus aureus but no T.B.. Calmette gave a negative reaction. He developed an Empyema and when the pus was ex-amined it was found to be purely pneumococcal. Calmette done again and was negative.

From this point he improved. Temperature kept normal and he felt well. The lungs however were not resolving as quickly as they should. So Calmette was done again and this time a positive reaction was obtained. This would show that the power of resistance of the lungs was so lowered the tubercular process got a footing in them.

Lymphadenoma:

Woman, 25, Complaint - Swollen glands in neck Axilla, Duration, 5 years. Condition started 5 years ago, 1st as a small hard lump on left side of neck to inner side of sterno-mastoid. Swelling gradually increased in size spreading upwards and backwards. Never any pain or inflammation. 2 years was treated with electricity in R. I. E. Considerable improvement, swelling became smaller. 2 years ago swellings made appearance on right side of neck, but have progressed very slowly. 3 or 4 years ago glandular swellings began to be noticed in left axilla Gone on enlarging since then, have now reached size of segment of cricket ball. On palpation swellings found to be made up of masses of lymphatic

'glands matted together. No tenderness. Dulness of left apex and front of chest down to 3rd rib. Has been feeling very tired and easily exhausted during last year. Sweats at night. Spleen greatly enlarged. Blood shows leucoytosis of 23,000 Lymthocytes 44 %. Calmette's reaction when tried gave an absolutely negative result.

Tabes Mesenterica followed by Tubercular Meningitis.

A. R. Boy, aged 8, a typical case of Tabes Mesenterica. After 8 months treatment he left hospital very much improved. He gave a positive reaction with Calmette. 6 weeks later re-admitted, complaining of very severe headache, giddiness, vomiting. Some retraction of head. Double Kernig, knee jerks, both exaggerated. Achilles ditto. Double Babinski. Pupils widely dilated, react normally. Internal Strabismus on both sides. No optic neuritis. 5th nerve on left side involved. Cerebro spinal fluid under great pressure, excess of small lymphocytes. No organisms. In-continence of urine and faeces. Calmette's reaction was negative. Died 14 days after admission. Post Mortem showed typical case of Tubercular Meningitis.

The interest in this case is the fact that Calmette's reaction was positive when suffering from Tabes Mesenterica and negative when the Meningitis set in. Other observers state that within a week before death, the reaction is negative. Others state that in all cases of Tubercular Meningitis there is a negative reaction. Calmette himself has got a reaction in cases of Tubercular Meningitis.

Tubercular Peritonitis:

Man, aged 23, Complaint - pains in stomach and bowels, diarrhoea. Duration, 6 months. Lost great deal of weight rapidly. Got a chill

which was followed in a fortnight by severe pain in the stomach and bowels, and diarrhoea. He sometimes has as many as 8 motions per day, and never less than 5.. On examination, abdomen prominent. A number of hard masses felt pretty well all over the abdomen. Keeps abdomen rigid. Pain on palpation. Some slight quantity of fluid in peritoneal cavity. Troubled with flatulence a good deal. Stools examined for T.B, but none were found. Calmette's reaction was negative in his case, probably due to the fact that the case was far advanced. In advanced cases there are 2 theories why the reaction is negative.

(1) During chronic Tuberculosis an antitoxin is developed and thus an immunity is imparted to the tissues.

(2) That the vitality of the patient is too low to give any inflammatory reaction.

Mitral Stenosis and Phthisis.

Girl, aged 17. Complaint shortness of breath, severe cough. Duration 2 years. History - very short of breath for the last 2 years. Nothing that she knows to account for it. She had scarlet fever 9 years ago Has had cough for the last year. Sweats at night.

When admitted was extremely short of breath and had a most troublesome cough. Has lost no weight. Says she always has slept with the windows open.

On examining her, she had a loud presystolic mitral murmur and a loud blowing murmur over the tricuspid area. Lungs: Left apex dull, slight increase V.R.and v.f.. High pitched bronchial breathing,crepitations. Calmette, well marked in 36 hours.

Under treatment her lung condition cleared up tremendously, but

the conjunctivitis was still visible 3 weeks after the reaction was done. The interest in this case is the fact that Mitral Stenosis and Phthisis are a rare condition in combination, and secondly the great improvement of her lung condition during the short time she was in hospital.

Tabes Mesenterica.

Girl, aged 8, admitted, complaining pain in abdomen, headache, sweating. Duration, 3 weeks. History, started having severe headaches and sweating at night 3 weeks ago. Her abdomen became very prominent. She refused to take any food. Her behaviour altered, never spoke to any one. Sat near the fire doing nothing. Got very thin. Previous health - always healthy. Family History - No tubercle in family. On admission, very pale faced, delicate looking child, poorly nourished, abdomen very prominent.

Alimentary System. On examining abdomen, very prominent and tense, distinct thrill on percussion showing a quantity of fluid to be present. Enlarged glands matted together in the neighbourhood of the umbilicus. Stools, pale. Lungs, no signs of Tubercle.

Blood - R. 3,120,000
Hgb. 42%
W. 5,200

Treatment- Hg Inunction Blaud's Pills 1 t.i.d.

Calmette' + in 5 hours and remained for about 10 days.

Addison's Disease.

Man, aged 26. Complaint, Pain and cold sensation passing from feet upwards, colour of face brownish and discolouration of lips.

Duration 4 months. History, 4 months ago took pains in his right side and occasionally vomited. One month later noticed his skin was much darker and that his lips were much discoloured - almost black. Very easily fatigued. Previous Health - Always a healthy man. On admission, brown skin on face, lower lip almost black. A number of pigmented moles on his arms. Palate, gums, inside of cheek along the course of the lingual arteries all pigmented. The nipples, genitals and axillae not markedly affected. Vaccination and other scars pigmented.

Blood pressure 130 Hg
Lungs, absolutely sound.
Urine, pale amber, no albumin.

Alimentary, Troubled with vomiting especially 15-20 minutes after food. Blood R 4,090,000, Hgb. 70% W 6,400

P 43% L 54% Eosin 3%

Nervous, General debility, easily tired.

Calmette + in 4 hours and lasted for about a fortnight.

Treated - Extract of Supra-renal gr. V. t.i.d.

The interest in this case is the fact that Addison's Disease is in many cases due to Tuberculosis of the Supra Renal Capsules and in this case there was absolutely no clinical evidence of tubercle.

Tubercular Peritonitis.

Boy, 8, extremely emaciated . Typical swinging temperature of advanced phthisis, with diarrhoea, prominent and boardlike abdomen. No evidence of tubercle in lungs. No T.B. found in stools. Gave negative Calmette reaction. He was undoubtedly suffering from advanced Tubercular Peritonitis.

Phthisis.

Boy, 12, signs of early phthisis at left apex. Gave positive reaction. This boy, (J. Redpath) is the brother of the boy who died of Tubercular Meningitis.

Phthisis.

Woman, 35, with marked pleurisy and consolidation of right apex. T.B. found in sputum. Calmette positive in 8 hours.

Pneumonia.

Woman, 52, with double pneumonia. Did not give positive reaction to Calmette. Lung did not clear up quickly and 3 weeks after admission she gave a positive Calmette reaction. T.B. found in sputum.

Phthisis and Tubercular Peritonitis.

Man 39 with advanced Phthisis of both lungs and Tubercular Peritonitis Gave negative Calmette reaction, due probably to far advanced Tubercular condition. Man died within a fortnight.

Phthisis.

Man, 51, with evidence of extensive tubercle of both lungs. Cavity at right apex and extensive consolidation. Two days after admission took a very bad fit of coughing and had a very severe haemoptysis which ended fatally. He did not give any reaction to Calmette. Post Mortem showed extensive tubercle with cavity formation.

Intracranial Tumour.

S. Boy, 13, with symptoms of intracranial tumour. Had double optic neuritis, vomiting, giddiness, etc., No evidence of tubercle in his lungs. Unfortunately his parents took him away before his case had been thoroughly gone into. Gave a positive Calmette reaction. Possibility of Tubercular Tumour in Brain.

Phthisis.

Man, 35, with early phthisis. Consolidation of right apex. T.B. found in sputum. Calmette positive in 8 hours.

Chronic Bronchitis, Asthma, Phthisis.

Man, 45, suffering from Asthma and Bronchitis. Slight dulness at right apex, and a few crepitations heard. No T.B. found in sputum. Calmette was positive in 10 hours and gave marked reaction.

Chronic Bright's, Phthisis.

Man, 35, suffering from Chronic Bright's. On examining his lungs, the whole of the left lung and the apex of the right were affected with tubercle. He did not give a positive reaction.

Tubercular Peritonitis, Addison's Disease, Phthisis.

Man, 32, markedly pigmented, extensive phthisis of both lungs and also tubercular peritonitis. Negative result.

Phthisis.

Man, 26, with symptoms and signs of early Phthisis. Consolidated left apex. A few T.B. found in sputum. Calmette positive in 6 hours, mild reaction.

Chronic Gastritis, Phthisis.

Man, 25, suffering from chronic gastritis. Had some cough and there were some physical signs of Phthisis. T.B. in sputum. Calmette positive.

Chronic Bronchitis, Asthma, Phthisis.

Man, 59, suffering from chronic Bronchitis, Asthma and a dilated heart. A few moist sounds and comparative dulness at right apex. No T.B. found in sputum. Calmette's reaction very well marked in 8 hours.

Aneurysm, Phthisis.

Man, 39, with physical signs of aneurism and also some dulness at one apex. Gave very marked reaction in 8 hours, which lasted a fortnight.

TABLE OF NEGATIVE CASES.

Sex.	Clinical Diagnosis.	Remarks.
	Diseases of Respiratory System.	
M.	Acute Lobar Pneumonia	No evidence of Tubercle.
M.	Acute Pleurisy	" " "
F.	Pleurisy with Effusion	" " "
M.	Chronic Bronchitis and Asthma	" " "
M.	Acute Lobar Pneumonia	" " "
M.	Acute Lobar Pneumonia	" " "
F.	Acute Lobar Pneumonia	" " "
M.	Broncho-Pneumonia	" " "
M.	Pleurisy with Effusion	" " "
M.	Acute Bronchitis	" " "
M.	Chronic Bronchitis	" " "
M.	Acute Bronchitis	" " "
M.	Acute Lobar Pneumonia	" " "
M.	" " "	" " "
F.	Broncho-Pneumonia	" " "
M.	Acute Lobar Pneumonia	" " "

Diseases of Respiratory System, Continued.

Sex.	Clinical Diagoisis.	Remarks.
M.	Broncho- Pneumonia.	No evidence of Tubercle.
F.	Acute Lobar Pneumonia	" " " "
M.	" " "	" " " "
M.	" " "	" " " "
M.	Pleurisy	" " " "
M.	Chronic Bronchitis	" " " "
M.	Acute Lobar Pneumonia	" " " "
F.	" " "	" " " "
M.	" " " P.M.	" " " "
F.	Chronic Bronchitis	" " " "
M.	Acute Lobar Pneumonia	" " " "
M.	" " "	" " " "

Diseases of Nervous System.

	Clinical Diagnosis.	Remarks.
M.	Disseminated Sclerosis	No evidence of Tubercle.
M.	Cerebral Thrombosis	" " " "
M.	Epilepsy	" " " "
M.	Progressive Muscular Atrophy	" " " "
M.	G. P. I.	" " " "
F.	Delusional Insanity	" " " "
F.	Chorea	" " " "
M.	Tabes Dorsalis	" " " "
M.	Disseminated Sclerosis	" " " "

Diseases of Nervous System, Continued.

Sex.	Diagnosis.	Remarks.
M.	Neurasthenia	No Evidence of Tubercle.
F.	Epilepsy	" " " "
F.	"	" " " "
M.	Disseminated Sclerosis	" " " "
F.	Spastic Paraplegia	" " " "
M.	Intracranial Tumour	" " " "
M.	Chorea	" " " "
M.	Progressive Muscular Atrophy	" " " "
F.	Neurasthenia	" " " "
M.	Tabes Dorsalis	" " " "
M.	Post Meningitis weakness	" " " "
M.	Traumatic Epilepsy	" " " "
F.	Chorea	" " " "
M.	Tabes Dorsalis	" " " "
M.	Sciatica	" " " "
F.	Intracranial Tumour	" " " "
F.	Spastic Paraplegia	" " " "
F.	Hemiplegia Aphasia	" " " "
M.	Disseminated Sclerosis	" " " "
F.	Hemiplegia	" " " "
M.	Disseminated Sclerosis	" " " "
F.	" "	" " " "
F.	Hemiplegia	" " " "
M.	Sciatica	" " " "
M.	Herpes Zoster	" " " "
M.	Poliencephalitis	" " " "
F.	Spastic Paraplegia	" " " "
M.	Poliomyelitis	" " " "
M.	Tabes Dorsalis	" " " "
M.	Alcoholic Neuritis	" " " "
M.	Cerebellar Disease	" " " "
M.	Sciatica	" " " "
M.	Spastic Paraplegia	" " " "
M.	Disseminated Sclerosis	" " " "
M.	Herpes Zoster	" " " "

Nervous Diseases, Continued.

Sex.	Diagnosis.	Remarks.
F.	Tabes Dorsalis	No Evidence of Tubercle.
M.	Epilepsy	" " " "
M.	Tabes	" " " "
M.	Syringo Myelia	" " " "
M.	Sciatica	" " " "
F.	Syringo Myelia	" " " "
M.	Poliomyelitis anterior acuta	" " " "
M.	Tabes Dorsalis	" " " "
M.	Chorea	" " " "
M.	Neuralgia of 5th Nerve	" " " "
M.	Progressive Muscular Atrophy	" " " "
F.	Chorea	" " " "
M.	Disseminated Sclerosis	" " " "
M.	Poliomyelitis anterior acuta	" " " "
M.	Traumatic Hemiplegia	" " " "
M.	Cerebral Haemorrhage	" " " "
F.	Epilepsy	" " " "
M.	G. P. I.	" " " "
F.	Religious Mania	" " " "
M.	Athetosis	" " " "
M.	Disseminated Sclerosis	" " " "
F.	Neuralgia	" " " "
M.	Disseminated sclerosis	" " " "
M.	Spastic Paraplegia	" " " "
M.	Preataxic Tabes	" " " "
M.	Friedreich's Ataxia	" " " "
M.	Sciatica	" " " "
M.	Disseminated Sclerosis	" " " "
M.	Monoplegia	" " " "
F.	Tabes Dorsalis	" " " "
M.	Disseminated Sclerosis	" " " "
M.	Tabes	" " " "
M.	Traumatic Neurasthenia	" " " "
M.	Disseminated Sclerosis	" " " "

Sex.	Nervous Diseases, Continued. Diagnosis.	Remarks.
M.	G. P. I.	No Evidence of Tubercle.
M.	Hemiplegia	" " " "
M.	Intracranial Gumma	" " " "
F.	Progressive Muscular Atrophy	" " " "
F.	Functional Hemiplegia	" " " "
M.	Aphasia	" " " "
M.	Facial Paralysis	" " " "
M.	Epilepsy	" " " "
F.	Hystero-Epilepsy	" " " "
M.	Melancholia	" " " "

	Diseases of Circulatory System. Diagnosis.	No Evidence of Tubercle.
F.	Mitral Incompetence	" " " "
M.	" "	" " " "
M.	Aortic Disease	" " " "
F.	Mitral Stenosis and Incompetence	" " " "
M.	" "	" " " "
M.	Aortic and Mitral Disease	" " " "
M.	Mitral Disease	" " " "
M.	Aortic and Mitral Disease	" " " "
F.	Mitral Incompetence	" " " "
M.	" "	" " " "
F.	" Stenosis	" " " "
F.	" "	" " " "
M.	Aortic Disease	" " " "
M.	Pericarditis	" " " "
M.	Endarteritis Obliterans	" " " "
M.	Aneurysm	" " " "
F.	Mitral Incompetence	" " " "
M.	Aneurysm	" " " "
F.	"	" " " "
F.	Mitral Incompetence	" " " "
M.	Aneurysm	" " " "
M.	Aortic Disease	" " " "

Sex.	Various Diseases.	
M.	Mastoid Disease	No Evidence of Tubercle.
F.	Exophthalmic Goitre	" " " "
M.	Melaena	" " " "
M.	Acute Bright's	" " " "
M.	Erysipelas	" " " "
M.	Subacute Bright's	" " " "
M.	Chronic Interstitial Bright's	" " " "
F.	Acute Gastric Ulcer	" " " "
M.	Influenza	" " " "
F.	Gastric Ulcer	" " " "
F.	Myxoedema	" " " "
F.	Floating Kidney	" " " "
M.	Acute Bright's	" " " "
M.	Exophthalmic Goitre	" " " "
F.	Cancer of Gall Bladder	" " " "
F.	Intestinal Obstruction	" " " "
M.	Exophthalmic Goitre	" " " "
F.	Typhoid	" " " "
F.	Chlorosis	" " " "
M.	Exophthalmic Goitre	" " " "
F.	Subacute Bright's	" " " "
F.	Gastric Ulcer	" " " "
F.	Dilated Stomach	" " " "
M.	Acute Gastritis	" " " "
F.	Gallstones	" " " "
F.	Chlorosis	" " " "
F.	Lumbago	" " " "
M.	Acute Bright's	" " " "
M.	Diabetes Mellitus	" " " "
F.	Uraemia	" " " "
M.	Pernicious Anaemia	" " " "
M.	Malignant Larynx	" " " "
M.	Filaria Loa	" " " "
M.	Acute Rheumatism	" " " "
F.	Carcinoma of Gall Bladder	" " " "
F.	Uraemia	" " " "
M.	Raynauds Disease	" " " "
M.	Megrim	" " " "

Sex.	Various Diseases, Continued.				
F.	Intracranial Tumour	No Evidence	of	Tubercle.	
M.	Subacute Bright's	"	"	"	"
M.	Chronic Bright's	"	"	"	"
M.	Acute Rheumatism	"	"	"	"
F.	Chlorosis	"	"	"	"
M.	Chronic Bright's	"	"	"	"
M.	Acute Tonsillitis	"	"	"	"
M.	Subacute Bright's	"	"	"	"
M.	Acute Rheumatism	"	"	"	"
M.	" "	"	"	"	"
M.	Gastritis	"	"	"	"
M.	Acute Bright's	"	"	"	"
M.	Lumbago	"	"	"	"
M.	Gastro-enteritis	"	"	"	"
F.	Floating Kidney	"	"	"	"
F.	Influenza	"	"	"	"
F.	Gastric Ulcer	"	"	"	"
M.	Acute Bright's	"	"	"	"
M.	Chronic Bright's	"	"	"	"
M.	Mucous Colitis	"	"	"	"
M.	Influenza	"	"	"	"
F.	Acute Rheumatism	"	"	"	"
M.	Haemophilia	"	"	"	"
M.	Chronic Bright's	"	"	"	"
M.	Lymphadenoma	"	"	"	"
F.	Subacute Bright's	"	"	"	"
F.	Chlorosis	"	"	"	"
F.	Mucous Colitis	"	"	"	"
M.	Addison's Disease	"	"	"	"
M.	Carcinoma of Liver	"	"	"	"
F.	Spleno Medullary Leukaemia	"	"	"	"
M.	Acute Bright's	"	"	"	"
M.	Diabetes Mellitus	"	"	"	"
M.	Chronic Dyspepsia	"	"	"	"
M.	Gastralgia	"	"	"	"
F.	Facial Paralysis	"	"	"	"
F.	Chlorosis	"	"	"	"

Sex.	Various Diseases, Continued.	
F.	Chronic Bright's	No Evidence of Tubercle.
F.	Obstruction of Bile Duct	" " " "
M.	Acute Bright's	" " " "
M.	Gastric Ulcer	" " " "
M.	Scurvy	" " " "
F.	Chronic Interstitial Bright's	" " " "
M.	Acute Gastritis	" " " "
F.	Acute Bright's	" " " "
F.	Gastric Ulcer	" " " "
F.	Chronic Gastritis	" " " "
M.	Carcinoma of Stomach	" " " "
M.	Scarlet Fever	" " " "
M.	Gastritis	" " " "
M.	Lumbago	" " " "
F.	Typhoid	" " " "

Before concluding, I should just like to mention a few important points in connection with the ophthalmo-reaction.

It is the aim of all Public Health Authorities to prevent the spread of Tuberculosis. One never picks up a medical paper without seeing some article on its prevention. This ophthalmo-reaction of Calmette's has proved itself wonderfully accurate, and if used systematically in schools, the medical man without much difficulty could separate out tubercular children from the others.

There is no doubt that if tuberculosis is to be kept from spreading, tubercular children in a household or community must be kept apart from those not affected.

Again it is all important to recognize tubercle early. The earlier the treatment is begun, the better results are obtained Often in

Surgery and Medicine when there is clinical evidence of Tubercle, it is too late for satisfactory treatment. What an easy thing for the practitioner to put a drop of Calmette's Test Solution into the eye and if he gets a positive result, he knows to keep his eyes open. Especially is this valuable in Tubercular families.

Every now and then one reads of the dangers of the Test. I myself have not had a bad result. Some medical men own that there was a lesion of the eye before the test was done, which explains for itself the bad results.

To make doubly sure of no bad results being got, first examine the eyes carefully. Then use a 1 in 200 Solution. If no reaction is produced by this very weak Solution, it is not conclusive that the person is not tubercular, but it is conclusive that by following the first instillation by a 1 in 150 or even 1 in 100 Solution the reaction is not likely to be so severe as to do any damage to the eye.

If on the other hand a positive reaction, however mild, is obtained with the 1 in 200 solution, it shows that the person is tubercular and that had a 1 in 150 or 1 in 100 solution been used, the reaction would have been very severe. I have heard of several doctors giving up the test as a result of having a mishap, but with care to the soundness of the eye and by using a 1 in 200 solution, I cannot see how any bad result can follow.

Of course there are fallacies, but these have been pretty satisfactorily explained. The advanced tubercular lesions giving a negative reaction has been explained thus:

(1) During Chronic Tuberculosis an antitoxin is developed and thus

an immunity is imparted to the tissues.

(2) Due to the fact that vitality is too low to give any inflammatory reaction.

Again negative results have been obtained in children where positive results were expected, due to the carelessness of the doctor in not seeing that the drop goes into the eye or due to the child crying and the tears washing the solution out of the eye. Such need not occur with due care on the part of the doctor.

In conclusion I unhesitatingly say that Calmette's Tuberculin Ophthalmo-Reaction has a great future in the diagnosis of Tubercle in man.
